Research on the HPV Vaccine: Update from the National Cancer Institute

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The National Cancer Program

Conduct and support cancer
Research
Training
Health information
dissemination

Goals 3 and 5 of the National Vaccine Plan



NCI's HPV Vaccine Research

Intramural research at NCI



International projects – Center for Global Health

Extramural funding, domestic



Intramural Research at NCI Costa Rica Vaccine Trial Long-Term Follow-Up

Primary aims:

- 1. Vaccine Protection (efficacy and immunogenicity): evaluate the protection afforded from the bivalent HPV vaccine, by time and dose
- 2. Clinical Impact: determine the total reduction in cervical pre-cancer resultant from vaccination

Secondary aims:

- 1. 10-year vaccine efficacy against HPV infection and disease
- 2. Minimum levels of antibodies required for protection
- 3. Duration of protection is similar at each anatomic site (cervix, anus, and oral region)

One or two vaccine doses (Cervarix, GSK) can induce 4 years of protection against persistent (6 months) HPV infection with HPV16/18

Number of doses: 1 dose

Vaccine arm	Number of Women	Number of events	Rate per 100 women	HPV vaccine efficacy (95% CI)
Control	380	24	6.3%	81 (63-94
HPV	HPV	422	5	81 (63-94

- Similar protection was seen against 12 month persistent infection
- It is unknown whether these results can be extrapolated to Gardasil

One or two vaccine doses (Cervarix, GSK) can induce 4 years of protection against persistent (6 months) HPV infection with HPV16/18 - 2

Number of doses: 2 doses

Vaccine	Number	Number	Rate per	HPV vaccine efficacy
arm	of Women	of events	100 women	% (95% CI)
Control	380	24	6.3%	81 (63-94
HPV	HPV	422	5	81 (63-94

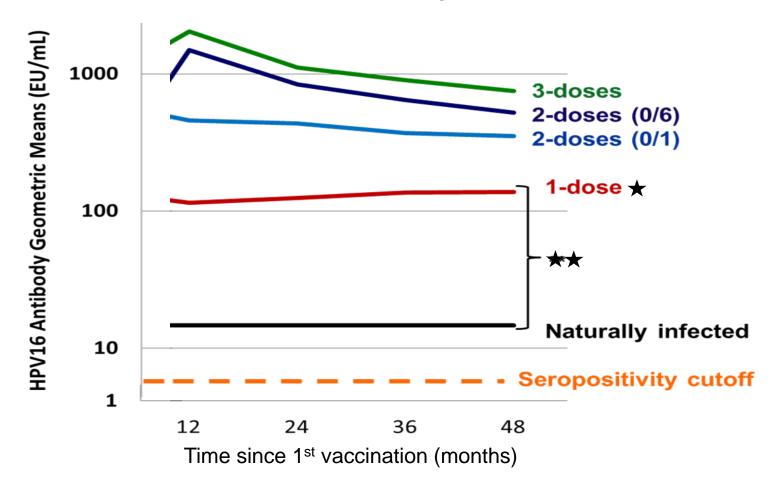
Number of doses: 3 doses

Vaccine arm	Number of Women	Number of events	Rate per 100 women	HPV vaccine efficacy % (95% CI)
Control	188	15	8.0%	100 (79-100)
HPV	HPV	196	0	100 (79-100)

- Similar protection was seen against 12 month persistent infection
- It is unknown whether these results can be extrapolated to Gardasil

Dose-stratified immunogenicity (4 yrs)

Cohort: CVT, HPV16/18 DNA negative at 1st vaccination



* 4-fold difference between 1 dose and 3 dose plateau titers ** 9-fold difference between 1 dose and natural infection plateau titers Safaeian M et al Cancer Prev Res 2013; 6:1242

Dose-stratified HPV16/18 VE (4 years)

Cohort: HPV16/18 DNA negative at 1st vaccination

Endpoint: Incident HPV16/18 infections

# of Doses	CVT	PATRICIA	
3	78% (73 to 82%)	77% (74 to 79%)	
2	77% (60 to 88%)	73% (40 to 89%)	
1	90% (75 to 97%)	72% (14 to 92%)	

Vaccine efficacy estimates lower than typically observed because of analytic cohort and endpoint— the key finding is that the observed efficacies are similar by dose

Stable Antibody Titers After 1 Dose

- There is no precedent for 1 dose of a protein-based sub-unit vaccine to induce stable antibody titers for several years
- May be attributable to two factors
 - VLPs are highly immunogenic
 - ASO4 is a TLR4 agonist
- A possible randomized controlled trial to rigorously test the efficacy of 1 dose

Test two commercial vaccines: one with alum, one with ASO4

Intramural Research at NCI Proposed Trial on Single Dose

- Direct evaluation of 2 and 1 dose regimens
- Data would be collected in Costa Rica and US
- Responsive to President's Cancer Panel recommendation to safely reduce number of doses

- Recognize that both options are off label in US
- Highly relevant to "real world" use in the US

Proposed Trial on Single Dose

Randomized Controlled Trial and Epidemiologic Study

Aim: Establish efficacy of 1 dose

- Four-arm trial: 1 and 2 doses of GSK and Merck (9-valent) vaccines
- Generate estimates of HPV infection among unvaccinated girls (Epidemiologic HPV survey)
- Initial phase: 4 years
- Long-term follow up: 10 years

Proposed Trial on Single Dose Randomized Controlled Trial

Location: Costa Rica

Population:

- Girls only, N=5000 per arm (20,000 total)
- Ages 13 to 16 years

Co-primary endpoints:

- 6-month HPV DNA persistence of vaccine related type
- HPV antibody titer and stability

Study visits every 6 months for 4 years, including questionnaire, blood and self-collected cervical sample (if sexually active) at each visit

Proposed Trial on Single Dose **Epidemiologic HPV Survey**

Location: Same regions of Costa Rica as girls in RCT and also US

Population: Ages 13 to 26 years, 500 per age category

Endpoint (same as trial):Incident 6-month HPV DNA persistence

Study Visits start in year 3 or 4, and occur every 6 months over 1 year (3 total study visits)

- Questionnaire, blood and self-collected cervical sample at each visit
- Offer HPV vaccination to survey subjects

International Projects Technical Support

- Gavi-eligible countries (Global Vaccine Alliance)
 - Using scientific evidence to inform vaccine policy
 - Implementation research
 - Strategic planning for cervical cancer prevention and control
- Cancer Control Leadership Forum Program helping countries develop and implement evidence-based comprehensive cancer control plans.
- Pink Ribbon Red Ribbon (PRRR) using PEPFAR platforms for prevention and control of cervical cancer, including HPV vaccination http://pinkribbonredribbon.org/

International Projects Advocacy

- August 2014 Asia Pacific Economic Cooperation (APEC)
 workshop with countries that have implemented HPV vaccine,
 including Australia, Malaysia, Peru, Philippines, Thailand
- Since 2012, dialog with Chinese public health officials and scientists conducting Chinese HPV vaccine research
- Worked to include HPV vaccine guidance in World Health Organization (WHO) non-communicable disease policy documents

Extramural Funding (1)

Center Grant Supplements
Opened to all 61 NCI-funded Clinical
Cancer Centers in August, 2014



40 applications received

Cancer Center Supplements

- 18 awards, up to \$150K for one year
- Purpose of awards:
 - Take advantage of local leadership
 - Gather local data on vaccine uptake, barriers, needs, collaborators
 - Create or increase local collaborations to promote HPV vaccine uptake

Extramural Funding (2)

- Of the 15 projects related to promoting uptake of the existing vaccines
 - 6 are developing and/or testing interventions to promote uptake
 - 3 are focused on how to communicate about the vaccine

 New announcements are in development, addressing President's Cancer Panel's call for research on communication about the HPV vaccine

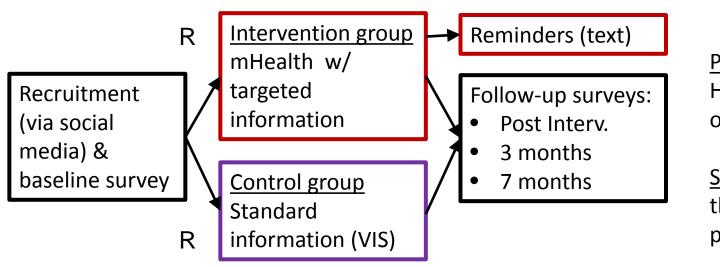


An mHealth HPV Vaccine Intervention for Young Gay & Bisexual Men (YGBM)

Aim 1: Develop intervention targeted to YGBM

- a) Conduct focus groups with YGBM
- b) Develop intervention materials for mobile platform
- c) Conduct review session with YGBM

Aim 2 & Exploratory Aim: Pilot test the intervention through an RCT with YGBM ages 18-26



Outcomes

<u>Primary</u>: Uptake of HPV vaccine series over 7 mo.

<u>Secondary</u>: Changes in theoretically-based potential mediators

NCI Supported HPV Vaccine Research

Safely reducing the number of doses needed

Supporting vaccine programs around the world

Defining and promoting high quality provider recommendations

Promoting local engagement and uptake across the US